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<110> Breitling, Frank
      Poustka, Annemarie
      Moldenhauer, Gerhard

<120> SELECTION OF MONOCLONAL ANTIBODIES

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<141> 2001-07-10

<150> PCT/DE00/00079
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taactagaga acccactgct tactggctta tcgaaattaa tacgactcac tatagggaga    660

cccaagcttg gtaccgagct cggatccact agtaacggcc gccagtgtgc tggaattcgg    720

cttggggata tccacc atg gag aca gac aca ctc ctg cta tgg gta ctg ctg    772
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ctc tgg gtt cca ggt tcc act ggt gac tat cca tat gat gtt cca gat    820
Leu Trp Val Pro Gly Ser Thr Gly Asp Tyr Pro Tyr Asp Val Pro Asp
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tat gct ggg gcc caa aag ccc gag gtg atc gat gcc agc gag ctg acc    868
Tyr Ala Gly Ala Gln Lys Pro Glu Val Ile Asp Ala Ser Glu Leu Thr
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ggc gag acc acc acc gag gcc gtg gac gcc gcc acc gcg gag aag gtg     964
Gly Glu Thr Thr Thr Glu Ala Val Asp Ala Ala Thr Ala Glu Lys Val
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ttc aaa caa tac gct aat gac aac ggg gtc gac ggc gag tgg act tac    1012
Phe Lys Gln Tyr Ala Asn Asp Asn Gly Val Asp Gly Glu Trp Thr Tyr
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gac gac gcc acc aag acc ttc acc gtg acc gag aag ccc gag gtg atc    1060
Asp Asp Ala Thr Lys Thr Phe Thr Val Thr Glu Lys Pro Glu Val Ile
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Asp Ala Ser Glu Leu Thr Pro Ala Val Thr Thr Tyr Lys Leu Val Ile
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Asn Gly Lys Thr Leu Lys Gly Glu Thr Thr Thr Glu Ala Val Asp Ala
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gcc gtc gac gga caa aac gac acc agc caa acc agc agc ccc tca gca    1348
Ala Val Asp Gly Gln Asn Asp Thr Ser Gln Thr Ser Ser Pro Ser Ala
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Ser Ser Asn Ile Ser Gly Gly Ile Phe Leu Phe Phe Val Ala Asn Ala
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65              70              75              80

Ala Asn Asp Asn Gly Val Asp Gly Glu Trp Thr Tyr Asp Asp Ala Thr
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Lys Thr Phe Thr Val Thr Glu Lys Pro Glu Val Ile Asp Ala Ser Glu
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Leu Thr Pro Ala Val Thr Thr Tyr Lys Leu Val Ile Asn Gly Lys Thr
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Leu Lys Gly Glu Thr Thr Thr Glu Ala Val Asp Ala Ala Thr Ala Glu
    130             135             140

Lys Val Phe Lys Gln Tyr Ala Asn Asp Asn Gly Val Asp Gly Glu Trp
145             150             155             160

Thr Tyr Asp Asp Ala Thr Lys Thr Phe Thr Val Thr Glu Ala Ala Ala
            165             170             175

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn Gly Ala Val Asp Gly
            180             185             190

Gln Asn Asp Thr Ser Gln Thr Ser Ser Pro Ser Ala Ser Ser Asn Ile
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Ala Ala Ala Leu Ala Pro Thr Gln Thr Arg Ala Gly Ala Gln Lys Glu
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aag acc ccc gag gag ccc aag gag gag gtg acc atc aag gcc aac ctg      807
Lys Thr Pro Glu Glu Pro Lys Glu Glu Val Thr Ile Lys Ala Asn Leu
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atc tac gcc gac ggc aag acc cag acc gcc gag ttc aag ggc acc ttc      855
Ile Tyr Ala Asp Gly Lys Thr Gln Thr Ala Glu Phe Lys Gly Thr Phe
        45                  50                  55

gag gag gcc acc gcg gag gcc tac cgc tac gcc gac gcc ctg aag aag      903
Glu Glu Ala Thr Ala Glu Ala Tyr Arg Tyr Ala Asp Ala Leu Lys Lys
    60                  65                  70

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Asp Asn Gly Glu Tyr Thr Val Asp Val Ala Asp Lys Gly Tyr Thr Leu
75                  80                  85                  90

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Asn Ile Lys Phe Ala Gly Lys Glu Lys Thr Pro Glu Glu Pro Lys Glu
                95                  100                 105

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Glu Val Thr Ile Lys Ala Asn Leu Ile Tyr Ala Asp Gly Lys Thr Gln
            110                 115                 120

acc gcc gag ttc aag ggc acc ttc gag gag gcc acc gcg gag gcc tac      1095
Thr Ala Glu Phe Lys Gly Thr Phe Glu Glu Ala Thr Ala Glu Ala Tyr
        125                 130                 135

cgc tac gcc gac gcc ctg aag aag gac aac ggc gag tac acc gtg gac      1143
Arg Tyr Ala Asp Ala Leu Lys Lys Asp Asn Gly Glu Tyr Thr Val Asp
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gtg gcc gac aag ggc tac acc ctg aac atc aag ttc gcc ggc aag gag      1191
Val Ala Asp Lys Gly Tyr Thr Leu Asn Ile Lys Phe Ala Gly Lys Glu
155                 160                 165                 170

aag acc ccc gag gag ccc aag gag gag gtg acc atc aag gcc aac ctg      1239
Lys Thr Pro Glu Glu Pro Lys Glu Glu Val Thr Ile Lys Ala Asn Leu
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Asp Asn Gly Glu Tyr Thr Val Asp Val Ala Asp Lys Gly Tyr Thr Leu
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Thr Ala Glu Phe Lys Gly Thr Phe Glu Glu Ala Thr Ala Glu Ala Tyr
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Val Ala Asp Lys Gly Tyr Thr Leu Asn Ile Lys Phe Ala Gly Ala Ala
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gga caa aac gac acc agc caa acc agc agc ccc tca gca tcc agc aac    1719
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ata agc gga ggc att ttc ctt ttc ttc gtg gcc aat gcc ata atc cac    1767
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Leu Phe Cys Phe Ser
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cagtctatta attgttgccg ggaagctaga gtaagtagtt cgccagttaa tagtttgcgc   4942

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<220>
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<400> 4

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            20                  25                  30


Lys Glu Glu Val Thr Ile Lys Ala Asn Leu Ile Tyr Ala Asp Gly Lys
        35                  40                  45
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Thr Gln Thr Ala Glu Phe Lys Gly Thr Phe Glu Glu Ala Thr Ala Glu
    50   55   60

Ala Tyr Arg Tyr Ala Asp Ala Leu Lys Lys Asp Asn Gly Glu Tyr Thr
65   70   75   80

Val Asp Val Ala Asp Lys Gly Tyr Thr Leu Asn Ile Lys Phe Ala Gly
            85   90   95

Lys Glu Lys Thr Pro Glu Glu Pro Lys Glu Glu Val Thr Ile Lys Ala
            100   105   110

Asn Leu Ile Tyr Ala Asp Gly Lys Thr Gln Thr Ala Glu Phe Lys Gly
        115   120   125

Thr Phe Glu Glu Ala Thr Ala Glu Ala Tyr Arg Tyr Ala Asp Ala Leu
    130   135   140

Lys Lys Asp Asn Gly Glu Tyr Thr Val Asp Val Ala Asp Lys Gly Tyr
145   150   155   160

Thr Leu Asn Ile Lys Phe Ala Gly Lys Glu Lys Thr Pro Glu Glu Pro
            165   170   175

Lys Glu Glu Val Thr Ile Lys Ala Asn Leu Ile Tyr Ala Asp Gly Lys
            180   185   190

Thr Gln Thr Ala Glu Phe Lys Gly Thr Phe Glu Glu Ala Thr Ala Glu
        195   200   205

Ala Tyr Arg Tyr Ala Asp Ala Leu Lys Lys Asp Asn Gly Glu Tyr Thr
    210   215   220

Val Asp Val Ala Asp Lys Gly Tyr Thr Leu Asn Ile Lys Phe Ala Gly
225   230   235   240

Lys Glu Lys Thr Pro Glu Glu Pro Lys Glu Glu Val Thr Ile Lys Ala
            245   250   255

Asn Leu Ile Tyr Ala Asp Gly Lys Thr Gln Thr Ala Glu Phe Lys Gly
            260   265   270

Thr Phe Glu Glu Ala Thr Ala Glu Ala Tyr Arg Tyr Ala Asp Ala Leu
    275   280   285

Lys Lys Asp Asn Gly Glu Tyr Thr Val Asp Val Ala Asp Lys Gly Tyr
    290   295   300

Thr Leu Asn Ile Lys Phe Ala Gly Ala Ala Ala Glu Gln Lys Leu Ile
305   310   315   320

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Ser Glu Glu Asp Leu Asn Gly Ala Val Asp Gly Gln Asn Asp Thr Ser
                325                 330                 335


Gln Thr Ser Ser Pro Ser Ala Ser Ser Asn Ile Ser Gly Gly Ile Phe
            340                 345                 350


Leu Phe Phe Val Ala Asn Ala Ile Ile His Leu Phe Cys Phe Ser
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<210> 5
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<400> 5

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gaccgcccaa cgacccccgc ccattgacgt caataatgac gtatgttccc atagtaacgc     180

caatagggac tttccattga cgtcaatggg tggactattt acggtaaact gcccacttgg     240

cagtacatca agtgtatcat atgccaagta cgccccctat tgacgtcaat gacggtaaat     300

ggcccgcctg gcattatgcc cagtacatga ccttatggga ctttcctact tggcagtaca     360

tctacgtatt agtcatcgct attaccatgg tgatgcggtt ttggcagtac atcaatgggc     420

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gtttgttttg gcaccaaaat caacgggact ttccaaaatg tcgtaacaac tccgccccat     540

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taactagaga acccactgct tactggctta tcgaaattaa tacgactcac tataggggaga     660

cccaagcttg gtaccggtgc g atg gca ccc tgc atg ctg ctc ctg ctg ttg      711
                         Met Ala Pro Cys Met Leu Leu Leu Leu Leu
                          1               5                  10

gcg gcc gcc ctg gcc ccg act cag acc cgc gcg ggg gcc caa aag ccc     759
Ala Ala Ala Leu Ala Pro Thr Gln Thr Arg Ala Gly Ala Gln Lys Pro
                15                  20                  25

gag gtg atc gat gcc agc gag ctg acc ccc gcc gtg acc acc tac aag     807
Glu Val Ile Asp Ala Ser Glu Leu Thr Pro Ala Val Thr Thr Tyr Lys
            30                  35                  40

cta gtg atc aac ggc aag acc ctg aag ggc gag acc acc acc gag gcc     855
Leu Val Ile Asn Gly Lys Thr Leu Lys Gly Glu Thr Thr Thr Glu Ala
        45                  50                  55

gtg gac gcc gcc acc gcg gag aag gtg ttc aaa caa tac gct aat gac     903
Val Asp Ala Ala Thr Ala Glu Lys Val Phe Lys Gln Tyr Ala Asn Asp
    60                  65                  70

aac ggg gtc gac ggc gag tgg act tac gac gac gcc acc aag acc ttc     951
Asn Gly Val Asp Gly Glu Trp Thr Tyr Asp Asp Ala Thr Lys Thr Phe
```

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       75                  80                    85                    90
acc gtg acc gag aag ccc gag gtg atc gat gcc agc gag ctg acc ccc     999
Thr Val Thr Glu Lys Pro Glu Val Ile Asp Ala Ser Glu Leu Thr Pro
                 95                  100                 105

gcc gtg acc acc tac aag cta gtg atc aac ggc aag acc ctg aag ggc    1047
Ala Val Thr Thr Tyr Lys Leu Val Ile Asn Gly Lys Thr Leu Lys Gly
                 110                 115                 120

gag acc acc acc gag gcc gtg gac gcc gcc acc gcg gag aag gtg ttc    1095
Glu Thr Thr Thr Glu Ala Val Asp Ala Ala Thr Ala Glu Lys Val Phe
             125                 130                 135

aaa caa tac gct aat gac aac ggg gtc gac ggc gag tgg act tac gac    1143
Lys Gln Tyr Ala Asn Asp Asn Gly Val Asp Gly Glu Trp Thr Tyr Asp
         140                 145                 150

gac gcc acc aag acc ttc acc gtg acc gag gcg gcc gca gaa caa aaa    1191
Asp Ala Thr Lys Thr Phe Thr Val Thr Glu Ala Ala Ala Glu Gln Lys
155                 160                 165                 170

ctc atc tca gaa gag gat ctg aat ggg gcc gtc gac gaa caa aaa ctc    1239
Leu Ile Ser Glu Glu Asp Leu Asn Gly Ala Val Asp Glu Gln Lys Leu
                 175                 180                 185

atc tca gaa gag gat ctg aat gct gtg ggc cag gac acg cag gag gtc    1287
Ile Ser Glu Glu Asp Leu Asn Ala Val Gly Gln Asp Thr Gln Glu Val
                 190                 195                 200

atc gtg gtg cca cac tcc ttg ccc ttt aag gtg gtg gtg atc tca gcc    1335
Ile Val Val Pro His Ser Leu Pro Phe Lys Val Val Val Ile Ser Ala
                 205                 210                 215

atc ctg gcc ctg gtg gtg ctc acc atc atc tcc ctt atc atc ctc atc    1383
Ile Leu Ala Leu Val Val Leu Thr Ile Ile Ser Leu Ile Ile Leu Ile
         220                 225                 230

atg ctt tgg cag aag aag cca cgt tcg tcg gcc gat cga gaa tcc atc    1431
Met Leu Trp Gln Lys Lys Pro Arg Ser Ser Ala Asp Arg Glu Ser Ile
235                 240                 245                 250

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gtgtcattct attctggggg gtggggtggg gcaggacagc aagggggagg attgggaaga   1671

caatagcagg catgctgggg atgcggtggg ctctatggct tctgaggcgg aaagaaccag   1731

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cgaccctgcc gcttaccgga tacctgtccg cctttctccc ttcgggaagc gtggcgcttt   2031

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<210> 6
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<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 6

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Thr Gln Thr Arg Ala Gly Ala Gln Lys Pro Glu Val Ile Asp Ala Ser
                20              25                  30


Glu Leu Thr Pro Ala Val Thr Thr Tyr Lys Leu Val Ile Asn Gly Lys
        35              40                  45


Thr Leu Lys Gly Glu Thr Thr Thr Glu Ala Val Asp Ala Ala Thr Ala
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```
              50                  55                  60

Glu Lys Val Phe Lys Gln Tyr Ala Asn Asp Asn Gly Val Asp Gly Glu
65                  70                  75                  80

Trp Thr Tyr Asp Asp Ala Thr Lys Thr Phe Thr Val Thr Glu Lys Pro
                85                  90                  95

Glu Val Ile Asp Ala Ser Glu Leu Thr Pro Ala Val Thr Thr Tyr Lys
               100                 105                 110

Leu Val Ile Asn Gly Lys Thr Leu Lys Gly Glu Thr Thr Thr Glu Ala
               115                 120                 125

Val Asp Ala Ala Thr Ala Glu Lys Val Phe Lys Gln Tyr Ala Asn Asp
       130                 135                 140

Asn Gly Val Asp Gly Glu Trp Thr Tyr Asp Asp Ala Thr Lys Thr Phe
145                 150                 155                 160

Thr Val Thr Glu Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp
               165                 170                 175

Leu Asn Gly Ala Val Asp Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu
               180                 185                 190

Asn Ala Val Gly Gln Asp Thr Gln Glu Val Ile Val Val Pro His Ser
       195                 200                 205

Leu Pro Phe Lys Val Val Val Ile Ser Ala Ile Leu Ala Leu Val Val
       210                 215                 220

Leu Thr Ile Ile Ser Leu Ile Ile Leu Ile Met Leu Trp Gln Lys Lys
225                 230                 235                 240

Pro Arg Ser Ser Ala Asp Arg Glu Ser Ile
               245                 250
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<210>  7
<211>  262
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Synthetic Construct

<400>  7
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1                5                  10                  15

Glu Arg Leu Phe Gly Tyr Asp Trp Ala Gln Gln Thr Ile Gly Cys Ser
                20                  25                  30

Asp Ala Ala Val Phe Arg Leu Ser Ala Gln Gly Arg Pro Val Leu Phe
```

```
                          35                  40                  45
```

Val Lys Thr Asp Leu Ser Gly Ala Leu Asn Glu Leu Gln Asp Glu Ala
    50   55   60

Ala Arg Leu Ser Trp Leu Ala Thr Thr Gly Val Pro Cys Ala Ala Val
65   70   75   80

Leu Asp Val Val Thr Glu Ala Gly Arg Asp Trp Leu Leu Leu Gly Glu
                85   90   95

Val Pro Gly Gln Asp Leu Leu Ser Ser His Leu Ala Pro Ala Glu Lys
                100   105   110

Val Ser Ile Met Ala Asp Ala Met Arg Arg Leu His Thr Leu Asp Pro
                115   120   125

Ala Thr Cys Pro Phe Asp His Gln Ala Lys His Arg Ile Glu Arg Ala
    130   135   140

Arg Thr Arg Met Glu Ala Gly Leu Val Asp Gln Asp Asp Gln Glu His
145   150   155   160

Gln Gly Leu Ala Pro Ala Glu Leu Phe Ala Arg Leu Lys Ala Ser Met
                165   170   175

Pro Asp Gly Glu Asp Leu Val Val Thr His Gly Asp Ala Cys Leu Pro
                180   185   190

Asn Ile Met Val Glu Asn Gly Arg Phe Ser Gly Phe Ile Asp Cys Gly
                195   200   205

Arg Leu Gly Val Ala Asp Arg Tyr Gln Asp Ile Ala Leu Ala Thr Arg
    210   215   220

Asp Ile Ala Glu Glu Leu Gly Gly Glu Trp Ala Asp Arg Phe Leu Val
225   230   235   240

Leu Tyr Gly Ile Ala Ala Pro Asp Ser Gln Arg Ile Ala Phe Tyr Arg
                245   250   255

Leu Leu Asp Glu Phe Phe
                260

<210> 8
<211> 286
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 8

Met Ser Ile Gln His Phe Arg Val Ala Leu Ile Pro Phe Phe Ala Ala
                              Page 16

```
1                    5                    10                   15

Phe Cys Leu Pro Val Phe Ala His Pro Glu Thr Leu Val Lys Val Lys
                20                  25                  30

Asp Ala Glu Asp Gln Leu Gly Ala Arg Val Gly Tyr Ile Glu Leu Asp
            35                  40                  45

Leu Asn Ser Gly Lys Ile Leu Glu Ser Phe Arg Pro Glu Glu Arg Phe
    50                  55                  60

Pro Met Met Ser Thr Phe Lys Val Leu Leu Cys Gly Ala Val Leu Ser
65                  70                  75                  80

Arg Ile Asp Ala Gly Gln Glu Gln Leu Gly Arg Arg Ile His Tyr Ser
                85                  90                  95

Gln Asn Asp Leu Val Glu Tyr Ser Pro Val Thr Glu Lys His Leu Thr
            100                 105                 110

Asp Gly Met Thr Val Arg Glu Leu Cys Ser Ala Ala Ile Thr Met Ser
            115                 120                 125

Asp Asn Thr Ala Ala Asn Leu Leu Leu Thr Thr Ile Gly Gly Pro Lys
    130                 135                 140

Glu Leu Thr Ala Phe Leu His Asn Met Gly Asp His Val Thr Arg Leu
145                 150                 155                 160

Asp Arg Trp Glu Pro Glu Leu Asn Glu Ala Ile Pro Asn Asp Glu Arg
                165                 170                 175

Asp Thr Thr Met Pro Val Ala Met Ala Thr Thr Leu Arg Lys Leu Leu
            180                 185                 190

Thr Gly Glu Leu Leu Thr Leu Ala Ser Arg Gln Gln Leu Ile Asp Trp
            195                 200                 205

Met Glu Ala Asp Lys Val Ala Gly Pro Leu Leu Arg Ser Ala Leu Pro
    210                 215                 220

Ala Gly Trp Phe Ile Ala Asp Lys Ser Gly Ala Gly Glu Arg Gly Ser
225                 230                 235                 240

Arg Gly Ile Ile Ala Ala Leu Gly Pro Asp Gly Lys Pro Ser Arg Ile
                245                 250                 255

Val Val Ile Tyr Thr Thr Gly Ser Gln Ala Thr Met Asp Glu Arg Asn
                260                 265                 270

Arg Gln Ile Ala Glu Ile Gly Ala Ser Leu Ile Lys His Trp
            275                 280                 285
```